O1

Age- and Sex-Matched Comparison of Viral Markers Among HTLV-I Carriers in Japan and Jamaica.

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Background: The risks of HTLV-I-assocaited diseases among carriers of this virus differ substantially across geographic areas. This observation may be due to differences in host immune response to HTLV-I infection, which may be reflected in the levels of viral markers.

Methods: We evaluated provirus load, antibody titer and presence of anti-Tax antibody in a total of 102 age-, sex-matched asymptomatic HTLV-I carriers from Japan and Jamaica, using standardized laboratory assays.

Results: The mean antibody titer (3.60 vs. 3.16 in log10, $P = 0.007$) and the detection of anti-Tax antibody (59% vs. 39%, $P = 0.05$) were higher in the Jamaican HTLV-I carriers than in the Japanese carriers. Provirus load was only marginally higher in the Jamaican subjects (3.07 vs. 2.96 in log10, $P = 0.08$).

Conclusions: Since provirus loads are similar in the Jamaican and Japanese HTLV-I carriers, differential risks of ATL and HAM/TSP across the two populations cannot be entirely explained by provirus load. While strong antibody responses to HTLV-I are likely the basis of a higher incidence of HAM/TSP in Jamaica, failure to mount antibody responses proportionate to the amount of provirus load may explain an increased risk of ATL in Japan. We speculate that distinct factors likely regulate antibody responses and provirus load.

O2

A Genome-Wide Scan Identifies Three Regions of Interest for a Locus Predisposing to HTLV-1 Infection in Childhood.

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Background: The aim of our study was a genome-wide scan to identify chromosomal regions linked to susceptibility to HTLV-1 infection (seropositive/seronegative status) in families of African origin living in a high endemic area.

Methods: A total of 5 pedigrees (61 subjects) were genotyped for 382 microsatellites markers spanning the entire genome. Genetic linkage analysis was performed using both a model-free and a model-based method. The latter approach used a dominant genetic model of transmission with almost complete penetrance by 10 years of age for carriers of the predisposing allele.

Results: Using both model-based and model-free analysis, one region provided evidence ($p = 0.001$, and $p = 2 \times 10^{-4}$, respectively) for linkage in the overall sample. Evidence for linkage was even stronger ($p = 9 \times 10^{-5}$, model-based analysis) when considering only the larger pedigree of the sample. Two additional regions were also found to provide suggestive evidence ($p < 0.004$) for linkage to HTLV-1 infection.

Conclusions: Refined mapping of the three identified regions with additional markers is ongoing. Nevertheless, these preliminary results suggest the existence of at least one major locus for the control of susceptibility to HTLV-1 infection in children (acquired through breast-feeding) living in an endemic population.

O3

Epidemiological and Molecular Data on 170 HTLV-II Cases of Italian IDUs.

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Background: The sera of 2800 intravenous drug users (IDUs) from Italian cohorts were tested for HTLV and HIV-1. About 80% were HIV-1+ and 6% HTLV-II+. Only five were HTLV-II mono-infected. 73 co-infected individuals, belonged to three different groups: 20 long term non progressors (LTNP) to AIDS, with elevated CD4 counts, no therapy; 31 slow progressors (SP) with substantial CD4 counts, under therapy; and 22 progressors (P) with low CD4 counts, under therapy.

Methods: The clinical and serological state of the three groups and of a subgroup of 12 co-infected individuals before and after HAART therapy was followed and the HIV-1/HTLV-II proviral load measured by Taqman PCR.

Results: The three groups were characterised by a distinct HTLV-II proviral load profile: higher than HIV-1 in LTNP, equal to HIV-1 in SP and lower than HIV-1 in P. For the subgroup of 12 co-infected cases, the HTLV-II proviral load tended to increase after starting the therapy, followed by a decrease upon continuation of therapy. In three mono-infected non-treated individuals it remained constant.

Conclusions: These results indicate that the HTLV-II proviral load in PBMCs of LTNP is elevated and significantly correlated to high CD4 counts. In individuals co-infected by HIV-1 and subjected to treatment, the HTLV-II proviral increased at the start of therapy whereas it remained constant with time for the HTLV-II mono-infected untreated individuals.

O4

Scanning the PTLV Genome for a Molecular Clock, Evolutionary Rates and Selective Pressures.

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Background: A full coding genome alignment was scanned for a molecular clock using the maximum likelihood framework in a sliding window approach.

Results: Under the clock model, systematic rates of evolution were estimated along the genome using the African/Melanesian PTLV-I separation as a calibration node. Although the molecular clock was significantly rejected for the full-length data set, we observed considerable variability in the likelihood ratio statistic along the genome. Only in the tax region, the molecular clock hypothesis could not be significantly rejected. The